

## **REMARKS**

### **Status of the Claims**

Claims 1-29 were pending.

Claims 1-29 were previously rejected.

Claims 1, 3, 4-6, 8, 10-13, 15, 17, 19, and 25 are amended herein.

Claims 7, 9, 14, 18, 20-21, 23-24, 26-27, and 29 are canceled.

Claims 30-54 are new claims.

Reconsideration is respectfully requested.

Applicant gratefully thanks Examiner Channavajjala for contacting the undersigned via telephone to expeditiously resolve this application. Below is a discussion of the double patenting rejections and terminal disclaimer, the claim amendments and new claims, and the Section 103 rejections.

### **Double Patenting Rejections and Terminal Disclaimer**

In the Office Action of July 28, 2003, claims 1-29 were rejected on provisional double-patenting grounds in view of US co-pending application Serial No. 10/055,653, assigned to the present assignee, now US Pat. 6,670,384 B2, which issued on December 20, 2003. Additionally, claims 15-29 were rejected on grounds of obviousness-type double patenting in view of US Pat. No. 6,576,651B2, also assigned to the present assignee.

During a telephonic interview with Examiner Channavajjala on or about March 29, 2004, applicant agreed to submit a terminal disclaimer with regard to both US Pat. 6,670,384 B2, and US Pat. No. 6,576,651B2. Accordingly, said terminal disclaimer is submitted herewith, and it is requested that these rejections be withdrawn.

### **Claims Amendments and New Claims**

The scope of the claims has been amended such that the claimed invention is now directed to compounds of formula I herein where "Q" is an epoxide. Thus, groups R<sup>8</sup>-R<sup>15</sup> are also deleted from the independent claims 1 and 15 as these variables pertain to groups where M is other than oxygen. The claims also have been amended to omit that the process is carried out under protection from light which inter alia, avoids any potential

overlap with US Pat. 6,670,384 B2 on statutory grounds. Further amendments are discussed below.

Claim 1 is further amended to 1) address antecedent basis issues (i.e., with regard to the *primary* lyophilized product of step b, as distinguished from the lyophilized product of step c), and 2) place in a dependent claim (now claim 30) the step of *packaging* the lyophilized product in a vial separate from the vial containing the reconstitution vehicle (now claim 30). As discussed during the interview with the Examiner Channavajjala on March 29, 2004, the claims as previously presented claimed less than the applicant was entitled to claim. Additionally, to this end, applicant has presented new claims 30-54, which are discussed further below.

Claims 3 and 4 are further amended to enhance the clarity of these claims with regard to the initial step of wetting and then the further step of adding water. These claims, as well as claims 5, 6, 13, 15, and 19, are also further amended to enhance the antecedent basis with regard to references to the "epothilone analog" versus "analog."

Claims 8 and 10 are amended to recite a range of temperatures and pressures as opposed to a specific numerical temperature or pressure. The inserted second value to establish these ranges were already recited in claim 1. Thus, the inclusion of the second value in these claims is not new matter.

Claims 11, 12 and 13 are amended to depend upon claims 30 and 32, for antecedent basis purposes. These claims further recite features related to the packaging step, and that step is now recited in claims 30-32, instead of claim 1.

Claim 15 is amended to recite the invention pertaining to the lyophilized epothilone analog wherein Q is an epoxide, and to omit from the scope of this claim numerical values for the concentration of epothilone analog and relative volume of surfactant and alcohol in the reconstitution vehicle. As discussed above, the claims as originally presented claimed less than the applicant was entitled to claim. Additionally, claim 15 is amended to recite that the second vial may contain a solvent mixture and to enhance antecedent basis with regard to the vials of the pharmaceutical preparation. Recitation of a solvent mixture is not new matter as the claims as originally presented recited a mixture of at least one surfactant and anhydrous ethanol.

Claims 17 and 19 are accordingly amended to enhance antecedent basis in view of the amendments to claim 15.

Claim 25 is amended for clarity to omit recitation of the formula for the epothilone analog because this claim is dependent upon claim 19 which incorporates by dependency the formula of claim 16. Thus, recitation of the formula in claim 25 was redundant.

New claims 30 through 33 recite features that previously were present in claims 1 and 15.

New claims 34 through 54 recite the invention in alternate ways. Each of these claims is directed to formulations and processes involving the compound of original claim 2. However, in these claims the invention is recited with various scope to which applicant is entitled. With regard to claims 34 through 37, the Examiner's attention is respectfully drawn to pages 12 through 14 of the specification which discuss various discoveries made by the inventors herein with regard to the epothilone analogs that are the subject matter of this invention, the difficulties encountered in seeking to compound a suitable formulation for these analogs, and the discoveries the inventors herein made in overcoming those challenges. For example, the claimed analogs have a tendency to degrade rapidly in aqueous environments. Applicants discovered that the stability and solubility of these epothilone analogs in formulation can be achieved upon lyophilization of a tertiary butanol solution of the analogs, advantageously prepared below ambient temperature. (Specification at pages 12-13). The subject matter of these claims is supported by the description at pages 12 through 14 of the specification and the original claims herein.

#### Section 103 Rejections

In the Office Action of July 28, 2003, Claims 1-29 were rejected under 35 USC § 103(a) over US Pat. No. 6,380,395 to Vite et al (hereinafter "Vite," which is assigned to the present assignee) in view of US Pat. No. 4,950,432 to Mehta. Additionally, during the telephonic interview on or about March 29, 2004, this rejection was further discussed with Examiner Channavajjala in view of US Pat. No. 6,605,599 to Vite et al.

It is believed the applicant has overcome this rejection in view of the differences in structure between the instantly-claimed compounds and those of Mehta.

**Fees**

Applicant has canceled eleven claims and added twenty-five new claims. The case now contains a total of four independent claims, but applicant originally paid a fee for five independent claims. Thus, a fee is due for fourteen new dependent claims. The Commissioner is authorized to charge the \$252 fee to Deposit Account No. 19-3880 in the name of Bristol-Myers Squibb Company as well as any additional fees that may be required.

**SUMMARY**

It is believed that all rejections of the claims have been addressed and that the instant claims are in condition for allowance. The Examiner is invited to contact the undersigned if it is believed a telephonic communication would expedite the prosecution of this application.

Respectfully submitted,



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